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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/671,764	09/27/2000	Joseph R. Piscgna	M-8978 US	7433

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/671,764	PISEGNA ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-10,20-29 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10,20-29 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-4, 6-10, 20-29 and 31 are pending.

Applicants' amendment filed February 23, 2004 is acknowledged, and applicants' response has been fully considered. Claims 1 and 3 have been amended, and claims 5, 11 and 12 have been cancelled. Therefore, claims 1-4, 6-10, 20-29 and 31 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claims 5, 11 and 12 under 35 U.S.C. § 112, first paragraph, is withdrawn in view of applicant's cancellation of the claim in the amendment filed in February 23, 2004.

3. The previous rejection of claims 1-12 under 35 U.S.C. § 112, second paragraph, is withdrawn in view of applicants' amendment to the claim, applicant's cancellation of the claim, and applicants' response at page 5 in the amendment filed in February 23, 2004.

Claim Rejections - 35 USC § 102

4. The previous rejection of claims 1-2, 5-7 and 11 under 35 U.S.C. 102(b) as being anticipated by Simon *et al.* (Aliment. Pharmacol. Therap. 4, 239-245 (1990)), is withdrawn in view of applicants' amendment to the claim, applicant's cancellation of the claim, and applicants' response at page 7 in the amendment filed in February 23, 2004.

5. The previous rejection of claims 1 and 12 under 35 U.S.C. 102(b) as being anticipated by Murphy *et al.* (U. S. Patent 4,997,950), is withdrawn in view of applicants' amendment to the

claim, applicant's cancellation of the claim, and applicants' response at page 8 in the amendment filed in February 23, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4, 6-10, 20-29 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for a method of increasing the efficacy of a gastric H^+/K^+-ATPase inhibitor (PPI) in a human in need of a PPI by administering an effective amount (e.g., 0.1-10 mg/kg/hr) of a pentagastrin, a gastrin or a gastrin analog in conjunction with the PPI, or a kit for the treatment of pathology characterized by excess gastric acid secretion, comprising a container containing a PPI, and a container containing a pentagastrin, a gastrin or a gastrin analog because the specification only discloses cursory conclusions without data supporting the findings, which state that the present invention provides a method of treating pathological conditions characterized by excess gastric acid secretion, in particular the method of administering a gastrin, a pentagastrin or an analog thereof in conjunction of a PPI, which will result in increased efficacy, or a kit for the treatment of pathology characterized by excess gastric acid secretion, comprising a container containing a PPI and a container containing pentagastrin (page 2, line 7-page 4, line 2). There are no indicia that the present application enables the full scope of the claim in view of a method of increasing the

efficacy of a PPI in mammal and a kit for the treatment of pathology of excess gastric acid secretion as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the presence or absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding analogs of gastrin or pentagastrin, and PPIs, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for administering pantoprazole to humans having pentagastrin (1 μg/kg/hr) - induced gastric acid secretion and monitoring the effect of pantoprazole in the inhibition of pentagastrin-induced gastric acid secretion (Example 1).

(3). The state of the prior art and relative skill of those in the art:

The related art (e.g., Simon *et al.* , Aliment. Pharmacol. Therap. 4, 239-245 (1990)) indicates the effect of a PPI, BY1023/SK&F 96022 on the pentagastrin-stimulated acid secretion in healthy male volunteers; Murphy *et al.* (U. S. Patent 4,997,950) teach the use of analogs from C-terminus of gastrin in adjunctive therapy with a PPI, omerprazole in animal models. However,

the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide teachings on administering an effective amount (e.g., 0.1-10 mg/kg/hr) of a pentagastrin, a gastrin or a gastrin analog in conjunction with a PPI, and the effect of the peptide in increasing the efficacy of the PPI in a human to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a method of increasing the efficacy of a PPI in a human in need of a PPI by administering an effective amount of a gastrin, a pentagastrin or a gastrin analog in conjunction with the PPI, or a kit for the treatment of pathology of excess gastric acid secretion, comprising a PPI and a gastrin, a pentagastrin or a gastrin analog, however, the in vivo effects of using an effective amount of gastrin, pentagastrin or a gastrin analog to increase the efficacy of a PPI are not adequately described or demonstrated in the specification, e.g., the specification indicates pentagastrin is an agent that is typically to increase acid secretion (page 2, lines 9-10), and PPIs are potent inhibitors of gastric acid secretion by inhibiting H^+/K^+-ATPase (page 2, lines 1-5), furthermore, Example 1 also indicates pentagastrin (1 μg/kg/hr) is administered continuously to induce hypersecretion in healthy subjects, and single doses of *i.v.* pantoprazole ranging 20-120 mg are found to suppress gastric acid secretion in a dose-dependent manner. However, the specification has not demonstrated an effective amount of pentagastrin such as 0.1-10 mg/kg/hr increases the efficacy of PPI in inhibiting gastric acid secretion as compared to the activity of using PPI alone, and it appears that the effect of pentagastrin with 0.1-10 mg/kg/hr in inducing gastric acid secretion in a human has not been considered in the combination therapy,

thus, the invention is highly unpredictable regarding the effect of pentagastrin in the inducing gastric acid secretion and increasing efficacy of PPI.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of increasing the efficacy of a PPI in mammal by administering a gastrin, a pentagastrin, or an analog of gastrin in conjunction with the PPI, or a kit for the treatment of pathology of excess gastric acid secretion, comprising a PPI and gastrin, or an analog of gastrin or pentagastrin. The specification indicates the pentagastrin can be administered before, simultaneously with or after the PPI administration with the general dosages (0.1-10 mg/kg/hr) for pentagastrin, gastrin, or analogs thereof (page 2), and Example 1 demonstrates single doses of *i.v.* pantoprazole ranging 20-120 mg suppressed gastric acid secretion in a dose-dependent manner in healthy subjects under continuous pentagastrin (1 μg/kg/hr) -induced hypersecretion. However, the specification has not demonstrated an effective amount (0.1-10 mg/kg/hr) of a gastrin, a pentagastrin, or an analog of gastrin increases the efficacy of a PPI as compared to the activity of PPI alone. Moreover, there are no working examples indicating the effects of gastrin, pentagastrin, or an analog thereof in increasing the efficacy of various PPIs in a human. Because pentagastrin has also an effect of inducing gastric acid secretion other than increasing efficacy of PPI, it is unpredictable about the effect of administering an effective amount of pentagastrin, gastrin or analog thereof on the gastric acid secretion. Since the specification fails to provide sufficient teachings on the use of gastrin, pentagastrin or various analogs thereof in conjunction with a PPI, and the in vivo effects of these peptides in increasing efficacy of PPI and inducing gastric acid secretion, it is necessary to have

additional guidance and to carry out further experimentation to assess the effects of gastrin, pentagastrin or various analogs thereof in the claimed method.

(6). Nature of the Invention

The scope of the claims encompasses a method of increasing the efficacy of a PPI in a human in need of a PPI by administering a gastrin, a pentagastrin or an analog thereof in conjunction with the PPI, but the specification has not provide sufficient teachings, nor has demonstrated using an effective amount of the peptide in conjunction with a PPI in the claimed method. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed methods, the effect of the variant is unpredictable, and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of using a gastrin, a pentagastrin or various gastrin analogs in the method of increasing efficacy of various PPIs.

In response, applicants indicate the specification has provided objective evidence that pentagastrin increases the efficacy of a typical PPI, and the Examiner has not offered objective evidence that pentagastrin, gastrin or gastrin analogs would fail function in a similar manner with other PPIs; to be enabling under 35 U.S.C. 112, first paragraph, a patent must contain a description that enables one skilled in the art to make and use the claimed invention, that some experimentation is necessary but not unduly extensive does not constitute a lack of enablement; and the factors considered in determining whether undue experimentation is required, are summarized in In re Wands, and the analysis of 8 factors indicates the practice of the claimed invention does not require undue experimentation, thus the rejection under 35 U.S.C. 112, first

paragraph should be withdrawn (pages 5-6 of the response). The response has been fully considered, however, the argument is not found persuasive because the specification only demonstrates pentagastrin at 1 μg/kg/hr is administered continuously to induce hypersecretion in healthy subjects, and single doses of *i.v.* pantoprazole ranging 20-120 mg are found to suppress gastric acid secretion in a dose-dependent manner. However, the specification has not demonstrated an effective amount (e.g., 0.1-10 mg/kg/hr) of pentagastrin, gastrin or any analog increases the efficacy of PPI in inhibiting gastric acid secretion as compared to the activity of using PPI alone, which are encompassed by the claims. Furthermore, there are no working examples indicating the effects of gastrin, pentagastrin, or an analog thereof in increasing the efficacy of various PPIs in a human, and it is unpredictable regarding the effect of administering an effective amount of pentagastrin, gastrin or analog thereof on the gastric acid secretion since pentagastrin has also an effect of inducing gastric acid secretion other than increasing efficacy of PPI. Since the specification has not provided sufficient teachings on the effect of pentagastrin, gastrin or analog thereof in increasing efficacy of PPI and inducing gastric acid secretion in the combination treatment, it is necessary to have further experimentation to assess the effects of pentagastrin, gastrin or analog thereof in the increasing efficacy of PPI.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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May 8, 2004

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